

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2005/001142

International filing date (day/month/year)
18.03.2005

Priority date (day/month/year)
19.03.2004

International Patent Classification (IPC) or both national classification and IPC
INV. C12N5/06 G01N33/574 C07K16/30 A61K39/395

Applicant
PROCURE THERAPEUTICS LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/001142

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:

☐ a sequence listing

☐ table(s) related to the sequence listing
 - b. format of material:

☐ in written format

☐ in computer readable form
 - c. time of filing/furnishing:

☐ contained in the international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/001142

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 26-31 and 56-65

because:

- ☒ the said international application, or the said claims Nos. 26-31 (Industrial Applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 56-65
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2005/001142

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-55, 66-74
	No: Claims	
Inventive step (IS)	Yes: Claims	1-55, 66-74
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-25, 32-55, 66-74
	No: Claims	26-31

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)

International application No.

PCT/GB2005/001142

1. Reference is made to the following documents:

D1: J. of Cell Science, Vol. 114, No. 21, 2001, pages 3865-3872,

D2: Cytometry, Vol. 54A, No. 2, 2003, pages 89-99,

D3: Blood, Vol. 90, No. 12, 1997, pages 5002-5012,

2. The present written opinion has been established with the assumption that the **priority date 19.03.04** is validly claimed. Therefore, document J. of Cell Science, Vol. 117, No. 16, 15 July 2004, pages 3539-3545, has not been considered to be part of the prior art as defined in the regulations (**Rule 64 (1) and (3) PCT**).

SECTION V

3. Novelty (Article 33(2) PCT)

The subject-matter of *invention 1* of the present application does not appear to be disclosed in the prior art as defined in the regulations (**Rule 64 (1)-(3) PCT**).

Therefore, in view of such prior art the subject-matter of **claims 1-55 and 66-74** of the present application has to be regarded as being new (**Article 33 (2) PCT**).

4. Inventive Step (Article 33 (3) PCT)

The **closest prior art** to evaluate the inventiveness of *invention 1* is any of documents **D1 or D2**, which disclose methods for the identification and isolation of human prostate stem cells.

Starting from any of **D1 or D2**, the underlying **technical problem** to be solved by *invention 1* of the present application can be considered to lie in the provision of an alternative method for the isolation of prostate stem cells.

The **solution** provided by the Applicant to solve the above problem is a method for the isolation of prostate stem cells comprising the selective enrichment of prostate stem cells which express CD133 antigen.

The method of **D1** comprises the selective enrichment of prostate stem cells which express the marker $\alpha_2\beta_1$ integrin.

D1 further indicates that the degree of enrichment of stem cells attainable by its method will allow further fraction and analysis of the stem cell population to identify a set of additional markers unique for prostate stem cells.

The method of **D2** comprises staining prostate stem cells with the fluorescent Hoechst 33342 dye. The isolated cells are subsequently investigated with existing markers of stem cell.

D2 refers that, although many prostatic stem cell markers have been proposed (PSCA - prostate stem cell antigen, PMSA - prostate specific membrane antigen, phosphoprotein p32), none are entirely tissue or location specific, and therefore there is a lack of an universally agreed prostatic stem cell marker.

The CD133 antigen, also known as AC133 antigen, has been identified as a marker for human haematopoietic stem and progenitor cells (**D3**).

There is no indication in the prior art that prostate stem cells express CD133 antigen nor that CD133 antigen can be used as a prostate stem cell marker.

Thus, there is no suggestion in the prior art that would teach the person skilled in the art to provide the method of *invention 1*.

Therefore, the subject-matter of *invention 1* (**claims 1-55 and 66-74**) of the present application is considered to involve an inventive step (**Article 33 (3) PCT**).

5. Industrial Applicability (**Article 33(4) PCT**)

5.1. The subject-matter of present **claims 1-25, 32-55, 66-74** is susceptible of industrial applicability as defined in **Article 33 (4) PCT**.

5.2. For the assessment of the present **claims 26-31** on the question whether they are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a

compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

SECTION VIII

6. The present application does not satisfy the criterion set forth in **Article 6 PCT** because the following claims are not clear.

6.1. **Claim 8**, which refers back to claims 1-7, states "...wherein said prostate derived tissue...". However, claims 1 and 2 do not mention a prostate derived tissue.

Claim 11, which refers back to claims 1-10, states "...wherein said collagen based matrix...". However, claims 1 and 2 do not mention a collagen based matrix.

Claim 16, which refers back to claim 15, states "...wherein said cloned cells...". However, claim 15 does not mention cloned cells.

6.2. **Claim 66** is directed to a non-human animal model, i.e. a product. However, due to the wording "... comprising the steps of...", the claim is drafted as a method claim.

This lack of clarity leaves a doubt regarding the category of claim 66.

The same is true for dependent **claims 67-71**.

6.3. The prostate stem cells used in the preparation of the non-human animal model (**claims 66-71**) and in the formation of vascularized prostate acini (**claims 72-74**) are not limited to the prostate stem cells of *invention 1*.

According to **Rule 6.3 (a) PCT** the definition of the matter for which the protection is sought shall be in terms of the technical features of the invention.

The subject-matter of **claims 66-74** should therefore be limited to the prostate stem cells of claims 12-14, as indicated for claims 38, 43, 45, 51 and 52.

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7. In case of filling amended claims, the applicant is requested to take account of the above comments.

The attention of the Applicant is drawn to the fact that the application may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed (**Article 34 (2)(b) PCT** and **Rule 70.2 (c) PCT**).

In order to facilitate the examination of the conformity of the amended application with the requirements of **Article 34 (2)(b) PCT**, the Applicant is requested to clearly identify the amendments carried out, irrespective of whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based.